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**REMARKS**

Applicants respectfully request that the amendments be entered in the claims. The amendments to the claims are entered to more particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

Applicants respectfully request that the amendments be entered at this time since they place the application in condition for allowance or substantially reduce the issues for appeal. The amendments are entered to bring to the Examiner's attention the full nature of the invention as set out at page 14, lines 5-15. Applicants respectfully submit that the amendment to the claims will not require a new search.

Before discussing the rejections over the prior art, Applicants deem it prudent to set forth what they consider to be their invention. The claims as amended are directed to a reaction medium for fermentation processes comprising: (a) a microorganism; (b) a phase inversion temperature emulsion, wherein the emulsion comprises water, an emulsifier and an oil phase selected from the group consisting of (i) fatty acid alkyl esters, vegetable triglycerides and mixtures thereof comprising a carbon source or transformant and, wherein, the emulsion has an average droplet size of from 50 to 400 nanometers. Claims 23-35 are directed to a fermentation process. The claims directed to the fermentation process have not been considered as directed to a nonelected invention. Applicants submit that the requirement for restriction is improper and untenable.

As presently claimed, the claims are directed to a fermentation medium and a process for carrying out the fermentation. That is, the fermentation medium and the

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method for utilizing the fermentation medium comprise only one invention. The common thread which ties the two inventions together is the use of a fatty carbon source in the form of a PIT emulsion. Since the fermentation medium is not taught or suggested by the references cited by the Examiner, the two sets of claims should be considered in one application.

The Examiner is well aware of the extremely high costs of obtaining and maintaining a patent. If the claims are not examined in one application, Applicants will be required to expend substantial financial resources and human resources in preparing and prosecuting the second application.

Claims 12-22 stand rejected under 35 USC 103(a) as being unpatentable over Inlow et al. (US 5,372,943) in view of Kopp-Holtwiesche (DE 3738812) and Forster et al. (WO 95/11660). Applicants respectfully submit that Inlow et al., Kopp-Holtwiesche and Forster et al. whether considered alone or in combination neither teach nor suggest the present invention.

Inlow et al. is directed to a lipid microemulsion which can be added to cell culture media to provide essential lipids in a bioavailable form and their components are disclosed. Applicants respectfully submit that the microemulsion disclosed in Inlow et al. and the amount added to the cell culture media would neither teach nor suggest the present invention. Inlow et al. disclose a microemulsion of a fatty material which fatty material is added to the culture media in an amount of 1 to about 50 mg/l of the culture medium. The emulsified fatty material also contains other micro nutrients such as cholesterol, alpha-

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tocopherol acetate, linoleic acid, and lecithin. As set forth at column 5, lines 7-15, the methyl esters, or the triglycerides are present in the medium in a concentration of from 1 mg/l to about 50 mg/l, preferably from about 5 mg/l to about 15 mg/l and most preferably about 10 mg/l. The fatty materials can also contain sterols in a concentration of from 2 mg/l to about 7 mg/l alpha-tocopherol in a concentration of 0.5 mg/l to about 4 mg/l, and preferably about 2 mg/l.

At column 12, lines 41-48, Inlow et al. teach:

"The reason lipids are supplied to the cells is not critical. They can be supplied as a microemulsion according to the invention whether they are considered as essential or growth promoting nutrients, physical or chemical protectants or as having other functions, as for example, as a solvolytic agent, as a membrane modifying agent, as a surface tension reducing agent and/or as a cell surface stabilizing agent."

Applicants submit that Inlow et al. would neither teach nor suggest that the microemulsion of the fatty material could be utilized as a carbon source in a culture medium. As shown in the examples, the small amount of the microemulsion added to the culture media substantially increased the growth rate of the cells in the culture. However, there is neither teaching nor suggestion that the microemulsion would be useful as the carbon source in the medium due to the small amount utilized. All of the examples utilize a "basal medium" which is described at column 10, lines 36-64. The "basal medium" is a nutrient mixture of inorganic salts, sugars, amino acids, optionally vitamins, organic acids and/or buffers. The sugars present in the "basal medium" are a source of carbon and the amino acids can be a source of nitrogen. There is no suggestion that the fatty material microemulsion could be substituted for the sugar as a carbon source.

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The deficiencies in Inlow et al. are not cured by combination with Kopp-Holtwiesche. Kopp-Holtwiesche discloses a fermentation process for preparing dodecanoic acid by the fermentation of a C12 carboxylic acid methyl ester. The lauric acid methyl ester is utilized as a transformant in which a terminal methyl group is oxidized in the fermentation medium to a carboxylic acid group for formation of dodecanoic acid. The Kopp-Holtwiesche reference does not cure the deficiencies in the teaching of Inlow et al.

Inlow et al. is directed to a culture medium for use in culturing cells which produce a protein which has some use or activity. Kopp-Holtwiesche is directed to a culture medium for transforming a lauric acid methyl ester to an ester of dodecanoic acid. Applicants respectfully submit that there is no teaching nor suggestion that adding the large amounts of the fatty acid to the Inlow et al. emulsion would provide a useful medium for preparing the expressed proteins of the reference. Applicants submit that it is clear that the Inlow et al. process requires micro quantities of the fatty microemulsions to increase the growth potential of the cell culture. The fatty acid microemulsion is not utilized as a carbon source in the growth medium.

The deficiencies in the combination of Inlow et al. with Kopp-Holtwiesche are not cured by combination with Forster et al. Forster et al. is directed to a cosmetic preparation which is an aqueous emulsion formed by the PIT method. The cosmetic emulsion of Forster et al. contains a cosmetic active agent selected from a group of deodorizing agents, perfume oils and light-protective factors (see abstract). Applicants submit that there would be no suggestion to include the cosmetic microemulsion of Forster et al. in the

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culture medium of Inlow et al. or Kopp-Holtwiesche.

As one skilled in the art of fermentation processes knows, the microorganisms to be cultured are very sensitive to the environment. This is particularly shown in Inlow et al. where the micro quantities of the microemulsion introduced into the culture medium substantially increases the rate of cell growth. Also, it is well known in the art that many substances have an adverse effect on the growth of microorganisms in a culture medium. Applicants submit that there is no suggestion that the addition of the cosmetic microemulsion disclosed in Forster et al. would be suitable for introduction into a culture medium as a carbon source. Applicant respectfully submit that there is no teaching or suggestion that the addition of the cosmetic microemulsion into the culture medium of Inlow et al., at a concentration much higher then that disclosed in Inlow et al., would lead to a useful culture medium, or that a carbon source such as sugar could be replaced by the fatty acid esters or fatty acid triglycerides of vegetable origin. Applicants respectfully submit that the combination of Inlow et al., Kopp-Holtwiesche and Forster et al. does not provide a prima facie case of obviousness for the invention.

In the Official Action at the bottom of page 2, the Examiner states that Forster et al. does not specifically address the intended use of the composition. Applicants submit that it is clear from the Abstract that the composition is a cosmetic composition containing organic cosmetic active agents. Applicants invite the Examiner's attention to the Abstract.

Applicants respectfully submit that to their knowledge, it is not a general or accepted practice to introduce substantial amounts of cosmetic materials into a culture medium.

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Applicants submit that the composition of culture media are closely controlled to provide for rapid multiplication of the cells in the culture and satisfactory generation of the desired product.

Since Inlow et al. utilize micro amounts of the microemulsion to increase the rate of proliferation of cells by supplying micro nutrients to the culture medium, coupled with Kopp-Holtwiesche which is directed to the use of lauric acid methyl esters to produce dodecanoic acid. Applicants respectfully submit there is neither teaching nor suggestion to introduce the lauric acid esters into the culture medium of Inlow et al. at the low concentrations required in Inlow et al. to transform the lauric acid methyl esters into the methyl ester of dodecanoic acid.

Applicants respectfully submit that as discussed above, Inlow et al. utilizes micro amounts of the fatty acid emulsion as a growth stimulant for the cells in the culture. Kopp-Holtwiesche utilize gross amounts of the lauric acid methyl ester as a transformant for the production of a methyl ester of dodecanoic acid. Applicants respectfully submit that there is neither teaching nor suggestion to introduce the large quantities of the lauric acid methyl ester into the culture medium disclosed in Inlow et al. Applicants therefore respectfully submit that the references are not combinable and a rejection based thereon is untenable.

As discussed above, Forster et al. is directed to cosmetic preparations formed by the PIT method. However, there is neither teaching nor suggestion that the cosmetic preparations containing the cosmetic ingredients would provide a culture medium which was friendly to the propagation of the desired microorganisms. As one skilled in the art

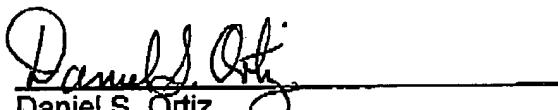
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understands, culture media are designed to provide for active growth of the microorganism and extraneous ingredients are not introduced in the culture media unless they are known to have a positive effect on the growth of the microorganism. Applicants submit that the microemulsion of Forster et al. with the cosmetic ingredients would not teach or suggest that the microemulsion could be introduced into a culture media without an adverse effect on growth of the microorganisms.

In view of the amendments entered in the claims and the above discussion, Applicants respectfully submit that the application is in condition for allowance and favorable consideration is requested.

Respectfully submitted,



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